REMARKS

In response to the office action mailed on July 10, 2008, Applicants submit the following remarks. Claims 1, 3-15, 17-27, 29-33, and 35-37 are pending.

The Examiner rejected claims 1, 3-10, 15, 17-27, 29-31 and 35-37 under 35 U.S.C. §103(a) as being unpatentable over Smith et al., US 5,888,930 ("Smith") in view of Gray, PCT/AU2001/001370 ("Gray"), in view of Kaminski et al., US 6,015,542 ("Kaminski").

Claims 1, 3-10, 15, 17-27, 29-31 and 35-37 cover particles that include a cross-linked polymer matrix. The particles have a first region including pores with a first predominant pore size. The particles also have a second region surrounding the first region. The second region has pores having a second predominant pore size. The first predominant pore size is larger than the second predominant pore size.

Smith does not disclose or render obvious such particles. Instead, Smith discloses a micro-porous particle made of a polymer that is soluble in a suitable solvent and insoluble in water. Smith describes his particle and the material suitable for making his particles as follows:

> The beads of the present invention are made of film-forming polymers, they have a generally spherical shape with diameters ranging from about 5 microns to about 5 mm, and they have a unique, continuously-gradated asymmetric microporous structure, with small pores near the surface and progressively larger pores toward the interior core. They are typically loaded with active ingredient following preparation of the beads, and the active ingredient is released at a slow and substantially constant rate over an extended period of time. (Smith, col. 2, lines 47-56.)
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> ***Useful polymers must be soluble in a suitable solvent and insoluble in a liquid that is miscible with the solvent.*** Typical polymer concentrations in the polymer solution are from 50 to 300 g/L. Solvents useful in the present invention must dissolve the polymer and be miscible with the liquid, typically water, used for precipitation. (Id., col.2, line 67-col.3, line 5; emphasis provided.)

To make the particles with the desired features, Smith further teaches a process that involves dissolving a polymer in a solvent other than water, spraying droplets of the resulting solution into a stirred precipitation bath that contains water, collecting the particles, and drying the particles. In this regard, Smith reads:

> The ***key*** to achieving the characteristic continuously-gradated asymmetric pore structure of the beads of the present invention is keeping the rate of solvent exchange with the liquid of the precipitation bath slow following a rapid initial precipitation that forms the "skin" layer. (Id., col. 3, lines 6-10; emphasis provided.)

> ***In order to achieve the continuously-gradated pore structure of the beads*** of the present invention, the polymer, its solvent, and the precipitation bath ***must all*** be specified. Examples of polymer/solvent bath combinations that result in asymmetric microporous beads of the invention include: polysulfone/dimethylformamide/water, polyvinylidenefluoride/dimethylformamide/water-dimethylformamide; polyvinylchloride/dimethylformamide/water dimethylformamide; polyurethane/dimethylformamide/water; and cellulose acetate/dichloromethane-dimethylformamide/water.
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> The beads of the present invention are prepared by first dissolving the polymer in a solvent or solvent mixture, then spraying droplets of the solution thus formed into a stirred precipitation bath containing a liquid, typically water, that is miscible with the solvent, allowing the precipitated beads to remain in the bath until substantially all of the solvent has been removed or exchanged, and then collecting the beads and drying them, if desired. (*Id.,* col. 3, lines 49-67; emphasis provided.)

Accordingly, after reading Smith, one skilled in the art would understand that, Smith's process does not involve forming a cross-linked polymer matrix. One skilled in the art would also understand that Smith discloses that his process, including, for example, the solvent, must be very carefully followed in order to obtain his particles with intended properties. As Smith explains:

> In summary, there is a need in the art for high strength sprayable granules or particles that can be prepared independently of loading with active ingredient, and that can release active ingredient at a constant rate over a prolonged period of time. (*Id.,* col. 2, lines 14-19; emphasis provided.)
>
> According to the present invention, asymmetric microporous beads are provided that can be prepared prior to loading them with active ingredient, that can contain up to 90% active ingredient, that are ***exceptionally durable and sprayable***, and that can release ***essentially all*** of the active ingredient ***at a constant rate over long periods of time***. ***These advantages are realized in part due to the asymmetric structure of the microporous beads, the asymmetry comprising a continuous gradation of pore sizes from very small pores near the surface to very large pores in the interior of the bead***. (*Id.,* col. 2, lines 21-32; emphasis provided.)

Thus, after reading Smith, it not only would not have been obvious to one of ordinary skill in the art to modify Smith's process to provide the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37, one skilled in the art would not have even wanted to try to modify Smith's process. Even if one skilled in the art had somehow tried to modify Smith to provide the particles covered by these claims, Smith would not have enabled a person to do so as Smith clearly does not disclose how to make such a particle with a cross-linked particle, let alone such a particle with the pore properties required by claims 1, 3-10, 15, 17-27, 29-31 and 35-37.

Gray does not cure Smith's deficiencies, at least because Gray does not disclose information that would have made one skilled in the art want to try to modify Smith's method to

provide the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37, and Gray also does not provide information that would have enabled one skilled in the art to make such a modification to Smith's process if such a person would have wanted to do so. Rather, Gray simply discloses a cross-linked particle with a radionuclide. (*See, e.g.,* Gray, p. 6, lines 11-17; p. 7, lines 13-17; p. 9, lines 7-12.) Gray does not even disclose how to make his particle, let alone how to modify it such that it would have the pore structure required by claims 1, 3-10, 15, 17-27, 29-31 and 35-37. In other words, neither Smith nor Gray provide an enabling disclosure of how to make the particles covered by these claims, and the combination of these references also does not provide an enabling disclosure for making such particles. Moreover, based on Smith, Gray or the combination of these references, one skilled in the art would not have even wanted to try to modify Smith's method to provide the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37.

Kaminski does not cure the deficiencies of Smith, Gray or the combination of Smith and Gray, at least because Kaminski does not disclose information that would have made one skilled in the art want to try to modify Smith's method to provide the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37, and Kaminski also does not provide information that would have enabled one skilled in the art to make such a modification to Smith's process if such a person would have wanted to do so.

None of Smith, Gray or Kaminski, alone or in combination, discloses or renders obvious the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37. Indeed, one skilled in the art simply would not have even tried to modify Smith's process based on the teachings of Gray or Kaminski to result in the particles covered by these claims. Further, none of the references cited by the Examiner, taken alone or in combination, enables a method that would result in the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37. Applicants therefore request reconsideration and withdrawal of this rejection.

The Examiner rejected claims 11-12 under 35 U.S.C. §103(a) as being unpatentable over Smith in view of Gray in further view of Ajay K. et al., *Extended preoperative polyvinyl alcohol microembolization of interacranial meningiomas: assessment of two embolization techniques*, AJNR 14, 571-582 (1993) ("Ajay"). Claims 11-12 cover particles that include a cross-linked polymer matrix. The particles have a first region with pores having a first predominant pore size.

The particles also have a second region surrounding the first region. The second region has pores with a second predominant pore size. The first predominant pore size is larger than the second predominant pore size. As discussed above, neither Smith nor Gray, alone or in combination, discloses or renders obvious such particles. Ajay does not cure the deficiencies of Smith and/or Gray, at least because Ajay does not disclose information that would have made one skilled in the art want to try to modify Smith's method to provide the particles covered by claims 11-12, and Ajay also does not provide information that would have enabled one skilled in the art to make such a modification to Smith's process if such a person would have wanted to do so. None of Smith, Gray or Ajay, alone or in combination, discloses or renders obvious the particles covered by claims 11-12. Indeed, one skilled in the art simply would not have even tried to modify Smith's process based on the teachings of Gray and/or Ajay to result in the particles covered by these claims. Further, none of the references cited by the Examiner, taken alone or in combination, enables a method that would result in the particles covered by claims 11-12. Applicants therefore request reconsideration and withdrawal of this rejection.

The Examiner rejected claims 13-14 and 32 under 35 U.S.C. §103(a) as being unpatentable over Smith in view of Gray in further view of Atcher et al., US 4,970,062 ("Atcher"). Claims 13-14 and 32 cover particles that include a cross-linked polymer matrix. The particles have a first region with pores having a first predominant pore size. The particles have a second region surrounding the first region. The second region has pores with a second predominant pore size. The first predominant pore size is larger than the second predominant pore size. As discussed above, neither Smith nor Gray, alone or in combination, discloses or renders obvious such particles. Atcher does not cure the deficiencies of Smith and/or Gray, at least because Atcher does not disclose information that would have made one skilled in the art want to try to modify Smith's method to provide the particles covered by claims 13-14 and 32, and Atcher also does not provide information that would have enabled one skilled in the art to make such a modification to Smith's process if such a person would have wanted to do so. None of Smith, Gray or Atcher, alone or in combination, discloses or renders obvious the particles covered by claims 13-14 and 32. Indeed, one skilled in the art simply would not have even tried to modify Smith's process based on the teachings of Gray and/or Atcher to result in the particles

covered by these claims. Further, none of the references cited by the Examiner, taken alone or in combination, enables a method that would result in the particles covered by claims 13-14 and 32.

The Examiner rejected claims 1, 3-15, 17-27, 29-33, and 35-37 on the ground of nonstatutory obviousness-type double patenting, citing eight commonly owned patent applications. In view of the other rejections to claims 1, 3-15, 17-27, 29-33, and 35-37, Applicants request that these rejections be held in abeyance.

Applicants believe that the claims are in condition for allowance, which action is requested.

Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 01194-458001.

Respectfully submitted,

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